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Sent: Friday, August 20, 2004 4:18 PM
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-----Original Message-----

From: Yaen, Christopher
Sent: Friday, August 20, 2004 4:05 PM
To: STIC-Biotech/ChemLib
Subject: 09705579

could you please get the following ref(s):

Nouv Rev Fr Hematol. 1989;31(2):77-84.

Cancer Chemother Biol Response Modif. 1991;12:67-73.

Onkologie. 1991 Feb;14(1):7-12.

Drugs. 1992;44 Suppl 4:1-16; discussion 66-9.

Semin Oncol. 1992 Dec;19(6):639-45.

Am J Health Syst Pharm. 1995 Jun 15;52(12):1287-304 quizz 1340-1.

Christopher Yaen
US Patent Office
Art Unit 1642
571-272-0838
REM 3A20
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CONTINUING EDUCATION



The ASHP Continuing Education System gives readers a self-assessment mechanism for selected articles in AJHP (and Clinical Pharmacy, within the time limits stated below). It allows readers to obtain continuing-education credit for these articles.

For the purpose of CE-credit enrollment, a blank answer sheet is published at the end of each installment of the column for the CE articles in that issue. An enrollee accumulates these answer sheets until the enrollment is submitted, using the form that is published in the June 15 and December 15 issues of AJHP. Any combination of tests within a three-year period may be included in an enrollment. More complete details about enrollment in the system appear in the semiannual enrollment form.

Article 680-204-95-007 (see page 1287)
Qualifies for 1.0 hour of CE credit

Vinorelbine: A novel vinca alkaloid

Learning objectives

After studying this article, the reader should be able to

1. Describe the chemistry, pharmacology, and pharmacokinetics of vinorelbine and compare them with those of other vinca alkaloids.
2. Identify malignancies against which vinorelbine has shown clinical activity.
3. Describe the adverse effects of vinorelbine.
4. State the FDA-approved indication for and dosage of vinorelbine.
5. Discuss alternative dosage regimens for vinorelbine.

Self-assessment questions

For each question there is only one best answer.

1. Compared with other vinca alkaloids, vinorelbine is reported to have
 - a. Broader antitumor activity.
 - b. A more favorable adverse-effect profile.
 - c. Narrower antitumor activity.
 - d. A more convenient dosage schedule.
 - e. Alternatives a and b are both correct.
2. The mechanism of action of vinorelbine is predominantly
 - a. Interference with microtubule assembly.
 - b. Interference with amino acids, cyclic adenosine 5'-
3. Which of the following statements about resistance to vinca alkaloids is (are) true?
 - a. Drug resistance among vinca alkaloids is mediated primarily by the multidrug resistance (*mdr*) gene.
 - b. Vinorelbine exhibits weak cross-resistance with vincristine and vinblastine *in vitro*.
 - c. The clinical efficacy of vinorelbine against vincristine- or vinblastine-resistant tumors is unknown.
 - d. Indirect evidence suggests that vinorelbine may be effective in breast cancer patients who have relapsed after treatment with anthracyclines.
 - e. All of the above alternatives are correct.
4. Which of the following statements about the pharmacokinetics of vinorelbine is false?
 - a. Vinorelbine is highly bound to various blood components, especially platelets.
 - b. The clearance of vinorelbine is approximately equal to the hepatic blood flow.
 - c. Vinorelbine pharmacokinetics are consistent with a three-compartment model.
 - d. Evidence of time dependence and dose dependence has not been reported.
 - e. A significant amount of vinorelbine elimination occurs through biliary secretion.
5. Vinorelbine was recently given FDA-approved labeling for use in patients with
 - a. Stage III non-small-cell lung cancer (NSCLC) in combination with cisplatin.
 - b. Stage IV NSCLC as a single agent or in combination with cisplatin.
 - c. Patients with metastatic breast cancer.
 - d. Alternatives a and b are both correct.
 - e. All of the above alternatives are correct.
6. Response rates for single-agent vinorelbine in previously untreated patients with NSCLC are
 - a. 70-90%.
 - b. 50-70%.

- c. 30-50%.
d. 10-30%.
e. Less than 10%.
7. Against which of the following malignancies has vinorelbine not shown any activity in preliminary studies?
 a. Breast cancer.
 b. Hodgkin's disease.
 c. Small-cell lung cancer.
 d. Head and neck tumors.
 e. Renal-cell carcinoma.
8. The FDA-approved dosage regimen for vinorelbine in NSCLC is:
 a. 30 mg/sq m i.v. once every three weeks.
 b. 60 mg/sq m i.v. once every three weeks.
 c. 30 mg/sq m i.v. once a week.
 d. 30 mg/sq m i.v. every two weeks.
 e. 30 mg/sq m/day i.v. for five days, repeated every three weeks.
9. The most frequent dose-limiting adverse effect of vinorelbine is
 a. Granulocytopenia.
 b. Nausea and vomiting.
 c. Peripheral neuropathy.
 d. Phlebitis.
 e. Thrombocytopenia.
10. Adjustment of the dosage of vinorelbine is recommended when
 a. The serum creatinine concentration is greater than 2 mg/dL.
 b. The granulocyte count is less than 1500 cells/cu mm.
 c. The total bilirubin concentration is greater than 2 mg/dL.
 d. There is grade 2 mucositis.
 e. Alternatives b and c are both correct.

Article 680-204-95-009 (see page 1323)
 Qualifies for 2.0 hours of CE credit

New approaches and technologies in drug design and discovery

Learning objectives

After studying this article, the reader should be able to

1. List the major approaches used by pharmaceutical companies in the drug discovery process.
 2. List the major challenges of rational, or structure-based, drug design.
 3. Describe the principal screening methods, technologies, and strategies used in drug discovery.
 4. Describe how antisense compounds would act as drugs.
5. List the combined capabilities of computer-assisted molecular design.
 6. List the interrelated components of molecular modeling.
 7. Describe the major techniques used in analyzing three-dimensional structures of complex proteins.
 8. List the advantages of small-molecule rational drug design.
 9. Describe the estimated costs of identifying a lead compound by traditional methods and successfully bringing a drug to the marketplace.

Self-assessment questions

For each question there is only one best answer.

1. New approaches and sophisticated technologies in the discovery and design of new drugs may result in all of the following except
 - a. Time and cost savings over the course of drug development.
 - b. Highly focused research with large molecular drugs.
 - c. Dramatic therapeutic advances in gene therapy.
 - d. Compounds that are more diverse but highly specific.
2. In 1993, the total cost for developing a newly marketed drug was
 - a. About \$100 million.
 - b. About \$1 billion.
 - c. More than \$350 million.
 - d. About \$1 million.
3. Which of the following statements about drug discovery and development in the United States is false?
 - a. The drug development process generally takes more than 10 years from the time of discovery to approval and marketing of a compound.
 - b. Biotechnology products have higher rates of successful development and approval than other drugs.
 - c. Improvements in the drug discovery process will be critical to the survival and success of pharmaceutical companies.
 - d. Random screening of compounds for the discovery of new drugs has become obsolete with the development of newer technologies.
4. The approaches to drug design used by pharmaceutical companies include
 - a. Modifications in structure based on testing the structure-activity relationship.
 - b. Design of selective compounds based on specific molecular interactions with receptors.
 - c. A hit-or-miss strategy based on random mass screening of synthesized compounds.
 - d. All of the above alternatives are correct.
5. Which of the following statements regarding the structure-based approach to drug design is false?
 - a. Computer-based imaging techniques can estimate the three-dimensional structure of human recep-